REMARKS

Claims 1, 4-12, 14, 15, 28, 30-36 and 43 are pending in the application. Claims 1, 7, 10 and 11 are currently amended.

Certain amendments are made to cure general objections raised by the examiner. The claim set has been numbered to show that claims 16-27 and 37-42 have been cancelled. Claims 10 and 11 have been amended as suggested by the examiner.

Claims 1, 2, 4-11, 14 and 15 stand rejected for indefiniteness under 35 U.S.C. §112 second paragraph. The Office asserts that the Specification on page 18 at lines 6-7 requires that AviIII polypeptides must provide a substrate binding activity or a cellulase activity, and so objects to the claims as written for filing to specify this activity. We respectfully traverse this requirement because the Office misinterprets the subject passage is not an exclusive definitional passage as interpreted by the Office. The subject passage does say that AviIII polypeptides *include* polypeptides having these activities; however, this is not expressly a definitional section and other polypeptides are not *excluded*. Therefore, the view of the Office is unduly limiting. A variety of other passages make this clear, for example, where the passage from page 18 at line 41 to page 19 at line 27 say that other AviIII polypeptides may also be included, and describes numerous ways of modifying SEQ ID NO. 1. It will be appreciated that the binding and cellulase functionalities which the Office presumes are not necessary for these compositions to have utility. Other utilities exist even for inactive AviIII polypeptides, for example, in the immune reactions described on page 20 at lines 10-26 and as the result of site directed mutagenesis as an informational approach to characterize or engineer the polypeptides as described on page 21 at lines 1-11. Therefore, we respectfully submit that the rejection

of claims 1, 2, 4-11, 14 and 15 is in error for the reasons discussed above and request withdrawal of the rejection.

Claim 7 has been amended to insert the word "comprising": which confirms that the polypeptide has the sequence of SEQ ID NO. 4.

Claims 1, 2, 4, 5, 14 and 15 stand rejected under 35 U.S.C. §112 first paragraph for want of enablement. The Office cites *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988) for a list of factors that pertain to undue experimentation and concludes that the specification does not enable those skilled in the art to make or use the invention in a manner that is commensurate with the scope of the claims. The Office explains that the claims recite percentages of identity, such as 70%, 80% and 90% identity with respect to the disclosed sequences, but those skilled in the art would not know how to make the variant polypeptides with the requisite activity and would also expect that such functionality would diminish with each substitution. We respectfully traverse for the reasons explained below.

To begin, the Applicant wishes to correct the Office perception, as is stated on page 5 of the Office Action, that the disclosure is limited to the polypeptide of SEQ ID NO. 1 (see claim 12). Applicant has amended claim 1 to show this is specifically not the case, and the specification is replete with statements to the contrary, such as the discussion of site-directed mutagenesis on page 18 at line 41 to page 21 at line 26. The Office finds that the results of protein modification are unpredictable; however, those skilled in the art understand that the unpredictability is mitigated by respecting the conserved residues as recited in claim 1. Furthermore, as has been discussed above, the Office mistakenly presumes that activity is required by the claims; however, it is not

required and even polypeptides that do not have the activity which the Office presumes are useful in characterizing the polypeptide through the types of studies that are discussed on page 21 at lines 1-11. Inactive polypeptides may also have uses as "unique epitopes" in producing antibodies and in assays as described on page 27 of the Specification.

The Office lists on pages 5-6 items (A) through (E) as factors that have affected the Examiner's decision to reject the claims. As to item (A), such activity is not required and even the inactive polypeptides have utility for the reasons explained above. As to item (B), the respecting of conserved residues is particularly claimed and this forms the guidance that the Office says is missing in item (E). Therefore, items (B) and (E) are untrue and in a true light are shown to be reasons actually favoring allowance of the claims. Item (C) again assets that activity is required, but it is not required. We fail to understand item (D) because applicant has provided this is a rational and predictable approach as is recited in claim 1, and this is more than sufficient in this art to eliminate undue experimentation.

The Office misapplies *In re Wands* to the extent that the Examiner is unwilling to tolerate what is a reasonable amount of experimentation in this art. At issue in Wands was whether a deposit of living cells was required to provide enablement for claims that addressed, broadly, a screening assay where IgM antibody had a binding affinity constant for HBsAg. The disclosure taught how to make and perform this assay from starting materials using mice, HBsAg antigen, and myeloma cells, but not from a universe of other materials. The Federal Circuit ultimately determined that enablement did exist for the broad concept, even where there was no deposit and the disclosed method taught narrowly the sole use of mice and myeloma cells. Thus, the analogy to *Wands* fails to the

extent the Office concludes that a wide-ranging disclosure of multiple embodiments and multiple means are always required to support broad claims, even genus claims, and that broad claims can never be supported by a single disclosed embodiment.

While the Wands factors are helpful, the factors merely guide one to a conclusion on the facts of each case. The ultimate issue is one of assessing reasonableness whether experimentation is undue in light of the state of the art and the level of ordinary skill. The factors are merely a guide towards this end and must consider the nature of the invention, as well as the *state of the art*. *Wands* states:

> Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. "the key word is 'undue,' not 'experimentation.' "
>
> The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art. *Ansul Co. v. Uniroyal, Inc.* 448 F.2d 872, 878-79; (2d Cir. 1971), *cert. denied*, 404 U.S. 1018 (1972). The test is not merely quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.
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> The term "undue experimentation" does not appear in the statute, but it is well established that enablement requires that the specification teach those in the art to make and use the invention without undue experimentation. Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations. The board concluded that undue experimentation would be needed to practice the invention on the basis of experimental data presented by Wands. These data are not in dispute. However, Wands and the board disagree strongly on the conclusion that should be drawn from that data.
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> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the

relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

In this art the level of skill is high. It is the nature of the art that those who modify proteins, for example, by site directed mutagenesis to perform protein engineering, cannot entirely predict the outcome; however, computational biology and other techniques as noted on page 21 at lines 1-11 may diminish the uncertainty in this regard. This type of routine unpredictability is merely the nature of the art, and so the experimentation is not undue. This is especially the case in view of the high level of ordinary skill.

Claims 1, 2, 4, 5, 14 and 15 stand rejected under 35 U.S.C. §112 first paragraph for lack of written description showing possession of the invention. It is the position of the Office that the Specification shows only a single disclosed species, but the claims address a genus including different proteins and partial peptide sequences. The Office concludes that the single disclosed embodiment is insufficient to place those skilled in the art in possession of the broader genus. We respectfully traverse for the reason that Applicant did disclose the broader genus that is recited in claim 1 and is shown to be in possession of what is claimed by the discussion of techniques for modifying protein structure, for example, in the passage from page 18 at line 41 to page 21 at line 26 of the Specification. If the Examiner believes that these techniques are not within the level of ordinary skill, then this should be specifically stated and explained because any such finding can be rebutted. The rejection cannot stand because it is contrary to the nature of the art and the level of skill.

Claims 1, 2, 4, 5, 14 and 15 stand rejected under 35 U.S.C. §112 first paragraph for lack of written description in that the claims recite new matter. This has been corrected by amendment to claim 1 now correctly referencing SEQ ID NO. 1 at the appropriate place. It will be appreciated that this amendment effectively broadens the claim because SEQ ID NO. 3 is a subset of SEQ ID NO. 1, and so the former recitation of SEQ ID NO. 3 was also not new matter.

Claims 1, 2, 4-12, 14 , 15, 28 and 43 stand rejected under 35 U.S.C. §103(a), as being unpatentable over Mohaghegi et al. 1986 in view of 'Berghem et al. 1976 and Katz et al. 1968. Mohaghegi et al. 1986 is said to show the isolation of *Acidothermus cellulolyticus*, but not the isolation of cellulase therefrom. Berghem et al. 1976 is used to show the isolation of an endoglucanase from *Trichoderma viride*. Katz et al. supposedly shows motivation to combine, since it is desirable to generate alternative cellulases capable of commercial scale processing at elevated temperatures. We respectfully traverse because the Office has not shown a *prima facie* case of obviousness.

"To establish prima facie obviousness of a claimed invention, all the claim limitations must be taught or suggested by the prior art." *See* MPEP 2143.03. At present, no reference teaches or suggests the GH74 family polypeptide that is claimed. This is an *exoglucanase* or modified exoglucanase, for example, as shown in SEQ ID NO. 1. In contrast, Mohaghegi et al. 1986 in view of Berghem et al. 1976 and Katz et al. 1968 uses Berghem et al. to show the isolation of a cellulase, but the cellulase is an *endoglucanase*. Therefore, this cannot be the GH74 family polypeptide that is claimed. As Paragraph 9 of the Rule 132 Declaration filed December 26, 2002 makes clear, the claimed GH74 domain functions as an exoglucanase, not an endoglucanase. It follows that the

combination does not teach or suggest all of the claim limitations because the combination, if proper, would merely result in the isolation of an endoglucanase from *A. celllulolyticus*. This does not teach the isolation of an *exoglucanase*. Exoglucanases are always much different in structure compared to endoglucanases. The difference is not as simple as the commonlity of "glucanase" terminology implies. This teaching with regard to expression of an endoglucanase does not generally apply to an exoglucanase.

The relevance of Bergheim et al., and Tan et al. to the instant rejection is unclear. In explaining the applied combination of references, the Office seems to say that the art teaches all of the things that Applicant used and did including the use of an Avicel assay, except for the isolation of the claimed polypeptide. If this is the case, perhaps it would have been obvious to try this methodology but isolation of the claimed exoglucanase would have been unexpected and the claimed polypeptide itself was unknown. Nothing in the combination of references teaches or suggests what is claimed.

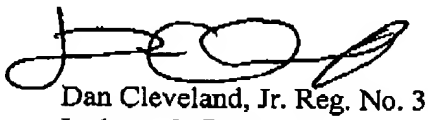
If the Office is asserting that the disclosed endoglucanase of the rejection was actually an exoglucanase as claimed, we disagree and it is the examiner's burden to prove this point by showing where the reference says this. A speculative reference of this nature cannot be used in support of a *prima facia* case, even assuming this is the position of the Office. The Applicant requests clarification of the rejection in this regard if this is what the Office intends, because the position, if asserted, would be contrary to well established law.

As discussed in Applicant's earlier response emphasizing the Declaration of Dr. Himmel, GH74 family sequences that are known to the art have no more than about 50% identity. The claims distinguish AviIII form the art by reciting 70%. Where a minimum

of 70% identity is particularly claimed with respect to SEQ ID NO. 1, this documents a substantial and nonobvious departure from the known sequences.

Applicants' attorney respectfully solicits a Notice of Allowance in this application. The Commissioner is authorized to charge any additionally required fees to deposit account 12-0600. Should the Examiner have any questions, comments, or suggestions that would expedite the prosecution of the present case to allowance, Applicants' representative, Paul White, earnestly requests a telephone call at (303) 384-7575.

Respectfully submitted



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